REMARKS

Claims 106-164 are pending in this application. By this amendment, claims 106-112, 138-139, and 161-162 are cancelled without prejudice or disclaimer, and claims 113, 114, 143, 148, 149, 151, 163, and 164 are amended. Following entry of this amendment, claims 113-137, 140-160 and 163-164 will be pending. Entry of this amendment is respectfully requested. Support for the amendments and new claims is found throughout the specification and originally filed claims, including, e.g., specification at page 13, lines 34-36. No new matter is added by this amendment.

With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any objection and/or rejection made by the Office. Applicants expressly reserve the right to pursue prosecution of any subject matter not presently claimed in one or more future or pending continuation and/or divisional applications.

Information Disclosure Statements

Applicants thank the Examiner for considering and initialing the PTO Forms 1449 that were mailed with the Office Action. Applicants note that a Supplemental Information Disclosure statement was mailed February 2, 2006. Consideration of the references submitted therein and return of an initialed PTO Form 1449 is respectfully requested.

Allowable claims; request for clarification of status of claim 152

Applicants note with appreciation that claims 113-114, 126-127, 130-134 and 153-160 are deemed allowable if rewritten in an independent form with all of the intervening claim limitations.

Claim 152 is not stated to be allowable, but is not rejected. Applicants would appreciate clarification regarding the status of this claim.

Withdrawal from allowance of previously allowed claims

Before issuance of this Office Action, claims 106-110, 138, 139, 147, 151, and 161-164 (corresponding to claims 8-16, 34, 36, 45, 49, and 102-105 in the Office Action mailed June 1, 2005 were deemed allowable subject matter by the Office and were accordingly **allowed**. Indeed, Applicants extensively amended and canceled the claims in the last Amendment in reliance on the allowance of those claims.

Withdrawal from allowance was not expressly acknowledged in this Office Action, but the previously allowed claims were rejected in the present Office Action. Applicants remind the Examiner that, according to the MPEP, "[g]reat care should be exercised in authorizing such a rejection" and

> [a] claim noted as allowable shall thereafter be rejected only after the proposed rejection has been submitted to the primary examiner for consideration of all the facts and approval of the proposed action. (MPEP § 706.04).

Applicants note that the Tan patent (USP 6,235,967) relied upon in the re-rejection of the claims was relied upon in prior Office Actions, and the Herlitschka patent (6,114,146) relied upon in the re-rejection of the claims was submitted to the Office in the IDS mailed October 18, 2004.

Objections

Claim 107 is objected for reciting the acronym "DHFR". Claim 107 has been cancelled, obviating the objection. Withdrawal of this objection is respectfully requested.

Claim 160 is objected to on the ground that is would allegedly be clearer if the term "where" and "is" were inserted in the position indicated in the Office Action. Claim 160 has been amended as suggested by the Examiner. Withdrawal of this objection is respectfully requested.

Claim 163 is objected to on the ground that the word "is" appears to be missing before the term "indicative". The claim has been amended as suggested by the Examiner. Withdrawal of this objection is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 106-111 and 143-150 are rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants respectfully disagree that the claims are unclear. However, to expedite prosecution, claims 106-111 have been cancelled, and claims 143, 148 and 149 have been amended and no longer reference a vector of claim 106. Accordingly, the rejection is moot and prompt withdrawal thereof is respectfully requested.

Rejection Under 35 U.S.C. § 102(b), or in the alternate, 35 U.S.C. § 103(a)

Claims 112, 143-146, 151 and 161-164 are rejected under 35 U.S.C. 102(b) as allegedly anticipated by or, in the alternative, under 35 U.S.C. 103(a) as allegedly obvious over Tan et al. (US 6,235,967)('967 patent). Applicants respectfully traverse this rejection.

102(b)

Claims 112, 143-146, 151 and 161-164 are rejected under 35 U.S.C. 102(b) as allegedly anticipated by Tan et al. (US 6,235,967). Applicants respectfully traverse this rejection.

Applicants additionally note that claim 112 has been cancelled, and claims 113 and 114, deemed allowable in the Office Action, have been rewritten in independent form. Claim 143 has been amended and no longer references a vector of claim 106. Claims 151, 163 and 164 have been amended and now recite that the desired product comprises a polypeptide. Claims 161 and 162 have been cancelled.

As a preliminary matter, Applicants disagree with the Examiner's interpretation of the term "operably linked". "Operably linked" is defined in the specification as follows:

> "Operably linked" refers to a juxtaposition of two or more components, wherein the components so described are in a relationship permitting them to function in their intended manner. **For example, a promoter and/or enhancer is operably linked to a**

> **coding sequence if it acts in cis to control or modulate the transcription of the linked sequence.** Generally, but not necessarily, the DNA sequences that are "operably linked" are contiguous and, where necessary to join two protein coding regions or in the case of a secretory leader, contiguous and in reading frame. However, although an operably linked promoter is generally located upstream of the coding sequence, it is not necessarily contiguous with it. Enhancers do not have to be contiguous. An enhancer is operably linked to a coding sequence if the enhancer increases transcription of the coding sequence. Operably linked enhancers can be located upstream, within or downstream of coding sequences and at considerable distances from the promoter. A polyadenylation site is operably linked to a coding sequence if it is located at the downstream end of the coding sequence such that transcription proceeds through the coding sequence into the polyadenylation sequence. Linking is accomplished by recombinant methods known in the art, e.g., using PCR methodology, by annealing, or by ligation at convenient restriction sites. If convenient restriction sites do not exist, then synthetic oligonucleotide adaptors or linkers are used in accord with conventional practice. (Specification, CITE)(emphasis added)

Examination of the rejected claims indicates that the term "operably linked" appears in the context of a promoter that is "operably linked" to a coding sequence. Applicants direct the Examiner's attention to the bold underlined text in the definition, which states "[f]or example, a promoter and/or enhancer is operably linked to a coding sequence if it acts in cis to control or modulate the transcription of the linked sequence." Thus, by the very language of the definition, a promoter that is "operably linked" to a coding sequence acts in cis to control of modulate the transcription of the linked sequence. Accordingly, it is evident that the term "operably linked" cannot encompass "any combination/positioning of the components on the vector, as long as the components function in their intended manner", as stated by the Examiner in the Office Action (pages 5-6).

Turning to the substance of the rejection, Applicants respectfully disagree that Tan inherently anticipates methods claims 151, 163 and 164. Applicants respectfully point out that the Examiner has not made a prima facie case for inherent anticipation under 35 U.S.C. § 102, and has not provided the required basis for alleging inherent anticipation. As such, the rejection does not stand.

The requirements for a rejection based on inherency are stated in M.P.E.P. § 2112, which describes the Examiner's burden in making such a rejection:

> In relying on the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. M.P.E.P. § 2112 (emphasis in original).

Moreover, "the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." Id. (quoting In re Oelrich, 212 USPQ 323, 326 (CCPA 1981).

The M.P.E.P. is in accordance with well-established case law addressing inherency. To serve as an anticipation when the reference is silent about the asserted inherent characteristic, the missing descriptive matter must be shown to be necessarily present in the thing described in the reference, and that it would be so recognized by the person of ordinary skill in the art. See *Continental Can Co. v. Monsanto Co.*, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). "Inherency may not be established by probabilities or possibilities," *In re Oelrich*, 212 USPQ 323, 326 (CCPA 1981), and "occasional results are not inherent." *Mehl-Biophile Int'l Corp. v. Milgraum*, 52 USPQ2d 1303, 1306 (Fed. Cir. 1999).

Accordingly, in order to make a prima facie case of inherent anticipation based on the cited reference, the Examiner is required to advance a basis in fact and/or technical reasoning to reasonably support the assertion that "expression of GFP and the amplifiable selectable marker are indicative of the cell also expressing VA1", as stated in the Office Action at page 9. However, the Examiner has not advanced any basis in fact and/or technical reasoning to support this assertion. And neither Tan nor Kaufman demonstrate that VA1 is expressed or that expression of GFP and DHFR are indicative of the cell also expressing VA1, as required by claims 151, 163 and 164. Accordingly, a prima facie case of inherent anticipation has not been made, and withdrawal of this rejection is respectfully requested.

Applicants further note that claims 151, 163 and 164 have been amended and now recite that the desired product comprises a polypeptide. By contrast, the adenovirus VA1 gene encodes an RNA polymerase III transcript that potentiates translation of the plasmid derived mRNA. (Kaufman, page 4486, right column). Thus, VA1 does not encode a polypeptide, and this Tan vector cannot anticipate the present claims. Withdrawal of this rejection is respectfully requested.

For the record, Applicants disagree with the Examiner's characterization of the Tan disclosure. Applicants respectfully direct the Examiner's attention to Applicants' remarks regarding Tan found in the Amendment filed March 8, 2005. Applicants further disagree that the "DHFR-GFP dicistronic vector" (GFP mobilization into pED-MTXr,) inherently discloses an IRES[1], because Kaufman states that EMC is a "putative" IRES (abstract), and that the EMC virus leader permits either internal initiation of translation or cryptic splice site in the EMC virus sequence permit production of mono-cistronic RNAs. A "putative" IRES, which may contain a cryptic splice site permitting function of mono-cistronic RNAs (as opposed to permitting internal initiation of translation) is hardly "necessarily, inevitably and always" an IRES, as required by the law and the MPEP. Accordingly, Applicants submit that the Examiner has not demonstrated that the EMC virus leader constitutes an IRES.

For the above-stated reasons, withdrawal of this rejection is respectfully requested.

103(a)

[1] Inherency requires that all of the limitations of the claims must be necessarily, inevitably, and always result from the prior art disclosure, and would be so recognized by one of ordinary skill in the art. M.P.E.P. § 2112. Moreover, "the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." *Id.*

Claims 112, 143-146, 151 and 161-164 are rejected under 35 U.S.C. 103(a) as allegedly obvious over Tan et al. (US 6,235,967)(Tan). Applicants respectfully traverse this rejection.

A prima facie case of obviousness has not been made. To establish a prima facie case of obviousness, three basic criteria must be met. First, the prior art reference(s) must teach or suggest all the claim limitations. Second, there must be some suggestion or motivation to modify the reference or to combine reference teachings. Third, there must be a reasonable expectation of success. See M.P.E.P. § 2143. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the Applicants' disclosure. See *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

The Examiner has not demonstrated that Tan teaches or suggests all the claim limitations, as noted above in response to the rejection under 35 U.S.C. § 102. Nor has the Examiner explained how Tan might be modified, such that Tan renders the present claims obvious. Finally, the Examiner has not explained how there might be a reasonable expectation of success. Thus, a prima facie case of obviousness has not been made, and withdrawal of this rejection is respectfully requested. Applicants note that claims 112, 161 and 162 have been cancelled and claim 143 has been amended and no longer references a vector of claim 106, thus obviating the rejection with respect to these claims. Withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 103(a)

Tan (US 6,235,967), further in view of Tan (US 2004/0191173)

Claims 112, 138-139, 143-147, 151 and 161-164 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Tan, et al. (US 6,235,967 as applied to claims 112, 143-146, 151 and 161-164 above, and further in view of Tan et al. (US 2004/0191173)(Tan '172 publication). Applicants respectfully traverse this rejection.

As a preliminary matter, Applicants that claims 112, 138, 139, 161 and 162 have been cancelled, and claims 113 and 114, deemed allowable in the Office Action, have been rewritten in independent form. Claim 143 has been amended and no longer references a vector of claim 106. Claims 151, 163 and 164 have been amended and now recite that the desired product comprises a polypeptide.

A prima facie case of obviousness has not been made. As noted above, Tan does not teach each and every limitation of the rejected claims. The Tan '173 publication is cited as allegedly teaching mammalian expression vectors using the CMV promoter. The Tan publication does not remedy Tan's deficiencies, and the Tan publication neither teaches nor suggests the claimed invention. Accordingly, withdrawal of this rejection is respectfully requested. Applicants note that claims 112, 138, 139, 161 and 162 have been cancelled, and claim 143 has been amended and no longer references a vector of claim 106 thus obviating the rejection with respect to these claims. Withdrawal of this rejection is respectfully requested.

Herlitschka (US 6,114,146), further in view of Tan (US 6,235,967)

Claims 106-109, 111, 112, 138-139, 143-151 and 161-164 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Herlitschka et al. (US 6,114,146) and further in view of Tan et al. (US 6,235,967, supra)(Tan). The Office Action states that it would be allegedly obvious to modify the fusion gene of Herlitschka to include GFP as a selectable marker, and cite the Tan patent as evidence that "a dicistronic vector encoding GFP is utilized to identify (i.e., select) cells that are expressing the GFP protein). (Office Action, page 13). Applicants respectfully traverse this rejection.

As a preliminary matter, Applicants that claims 112, 138, 139, 161 and 162 have been cancelled, and claims 113 and 114, deemed allowable in the Office Action, have been rewritten in independent form. Claim 143 has been amended and no longer references a vector of claim 106. Claims 151, 163 and 164 have been amended and now recite that the desired product comprises a polypeptide.

A prima facie case of obviousness has not been made. To establish a prima facie case of obviousness, three basic criteria must be met. First, the prior art reference(s) must teach or suggest all the claim limitations. Second, there must be some suggestion or motivation to modify the reference or to combine reference teachings. Third, there must be a reasonable expectation of success. See M.P.E.P. § 2143. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the Applicants' disclosure. See *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

(1) The Examiner has not demonstrated that each and every limitation of methods claims 151, 163 and 164 are taught or suggested in the cited references. For example, claims 151, 163 and 164 require that "expression of the GFP and the amplifiable selectable marker is indicative of the cell also expressing the desired product". This limitation, however, is not addressed in the rejection. Accordingly, a prima facie case of obviousness has not been made, and withdrawal of this rejection is respectfully requested.

(2) Herlitschka does not disclose a vector comprising a fusion gene comprising a selectable gene and an amplifiable gene. Herlitschka is cited as allegedly teaching

> a vector (i.e., polynucleotide) comprising a promoter, a foreign gene (i.e. selected sequence encoding a desired product) and a fusion gene comprising a first selectable gene and an amplifiable gene . . . (Office Action, page 11).

By contrast, Herlitschka discloses a vector comprising a fusion gene encoding two amplifiable selectable markers: DHFR and *hph*, the gene encoding resistance to hygromycin. Herlitschka teaches that this system permits use of methotrexate as a dominant selectable marker in dhfr+ cells, which Herlitschka characterizes as a previously unaddressed problem.

Specifically, Herlitschka teaches that:

> [a] surprising result was obtained that also the hygromycin B phosphotransferase gene is amplifiable. (Emphasis added; col. 8, lines 9-11)
>
> and
>
> [t]he dihydrofolate reductase gene/hygromycin B phosphotransferase gene system offers the particular advantage that on account of the tight coupling of the hph and dhfr domains, this fusion protein can be amplified as a dominant marker also in cells having endogenous dhfr gene. This is particularly enabled by the property of hph amplification potential so that one can speak of a double-dominant selectable and double amplifiable marker protein. (Emphasis added; col. 6, lines 20-27)
>
> and
>
> at first a sufficiently high hph amplification can be effected which ensures in the subsequence switching to MTX that the MTX concentration which is selected then, can no longer by compensated by endogenous DHFR. (Emphasis added; col. 6, lines 27-31).

Applicants acknowledge that Herlitschka mentions a "selection marker" in the specification. But the only disclosure in Herlitschka of "selection markers" suitable for use in the invention is *hph*, and Herlitschka explicitly states that *hph* is an amplifiable selection marker. Accordingly, it is evident that Herlitschka discloses a vector comprising a fusion gene encoding two amplifiable selectable markers, not a vector comprising a promoter, a foreign gene (i.e. selected sequence encoding a desired product) and a fusion gene comprising a first selectable gene and an amplifiable gene as stated in the Office Action. Withdrawal of this rejection is respectfully requested.

(3) Moreover, one of ordinary skill in the art would lack motivation to combine Herlitschka with the Tan patent. One of ordinary skill would not be motivated to substitute non-amplifiable selectable markers, such as GFP, into the vector of Herlitschka, since Herlitschka describes vectors comprising two amplifiable selectable markers. Withdrawal of this rejection is respectfully requested.

(4) The Examiner has also not demonstrated that there is a reasonable expectation of success. The reasonable expectation of success must be founded in the prior art, not in the Applicants' disclosure. *See In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). By contrast, in the rejection, the Examiner merely states that "given the level of skill in the art at the time of invention, there would have been a reasonable expectation of success in making such a modification, because the steps for making such a modification would have entailed nothing more than routine molecule biology" (Office Action, page 13). The Examiner does not explain, however, how the prior art provides a reasonable expectation of success. A high level of skill in the art, as cited by the Examiner, does not overcome this deficit. The fact that a claimed invention is allegedly within the capabilities of one of ordinary skill is not sufficient to establish prima facie obviousness. *See* MPEP 2143.01. Withdrawal of this rejection is respectfully requested.

Applicants further submit that there was no reasonable expectation of success. As noted in the specification at page 9, lines 1-5,

> initially, the integrity of the integrated expression vector and of the transcriptional linkage between the product gene of interest and the amplifiable gene as well as the GFP reporter gene upon amplification, was not predictable. It was possible that the gene of interest and/or the GFP gene may be deleted during amplification, as was previously reported with the DHFR gene (Kaufman et al. Mol. & Cell. Biol. 12: 1069-1076 (1981); Kaufman and Sharp, J. Mol. Biol. 159:601-621 (1982).

Moreover, Applicants respectfully submit that there was no reasonable expectation of success that expression of the GFP and the amplifiable selectable marker would be indicative of the cell also expressing the desired product, as is required in methods claims 151, 163 and 164. Withdrawal of this rejection is respectfully requested.

For the record, Applicants respectfully disagree with the Examiner's overbroad interpretation of the term receptor. Applicants submit that one of skill in the art would not interpret the term "receptor" to encompass Factor VIII, a secreted glycoprotein found in plasma. Applicants also disagree that the Examiner has made a prima facie case that an intron providing a splicing efficiency of at least 95% is inherently disclosed in Herlitschka.

For the above-stated reasons, withdrawal of this rejection is respectfully requested. However, Applicants note that claims 112, 138, 139, 161 and 162 have been cancelled, claims 113 and 114, deemed allowable in the Office Action, have been rewritten in independent form, and claim 143 has been amended and no longer references a vector of claim 106, thus obviating the rejection with respect to these claims. Withdrawal of this rejection is respectfully requested.

Double Patenting

Application No 10/714,000

Claims 106-111, 115-125, 128-129, 135-143, 148-152, 161-164 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 59-71 and 80-92 of co-pending Application No 10/714,000 ('000 application) in view of Tan et al. (US 6,235,967). Applicants respectfully traverse this rejection for the reasons stated below. However, Applicants additionally request that this provisional rejection be placed in abeyance until allowable subject matter has been found.

A prima facie case of obviousness-type double patenting has not been made. In an obviousness-type double patenting analysis, the Examiner must compare what is defined by the claims of the later application against what is defined by the claims of the earlier application. This analysis must be based on the claims as a whole, not one feature or element of the claims considered in isolation. *See, e.g. General Food Corp. v Studiengesellschaft Kohl mbH*, 972 F2d 1272, 1278-79 (Fed. Cir. 1992 ("Claims

must be read as a whole in analyzing a claim of double patenting"); *Eli Lilly v Barr Labs, Inc.*, 251 F3d 955, 972 (Fed. Cir. 2001) ("We compared the differences between the claims at issue as a whole and conclude that they are not patentably distinct") (emphasis added).

In other word, the compositions and methods as defined by *all the required* limitations of the claims of the '586 application must be compared to the compositions and methods as defined by *all the required* limitations of the claims of the instant application. It is improper to compare only one step or limitation found in claims of the instant application and claims of the '000 application, and to ignore additional limitations required by the claims of the instant application.

The Examiner has not explained why the inventions defined by claims 106-111, 115-125, 128-129, 135-143, 148-152, and 161-164 would be considered "obvious" in view of the inventions defined by claims 106-118, 122-152 and 161-164 of the '000 application. Instead, the Examiner relied upon the comparison of individual steps or limitations found in the independent claims of the instant application and the independent claims of the '000 application (eg, vector and polynucleotide, GFP and selectable gene), concluding that

> The only difference between the claims is that the instant claims are directed to a vector versus a polynucleotide in the reference claims and that the instant claims are delimited to a particular selectable marker-GFP, which is well recognized as a selectable marker, as is taught by the '967 patent. (Office Action, page 16).

Because the Examiner did not compare the claims as a whole, and instead compared features or elements of the claims considered in isolation, a *prima facie* case of obviousness-type double patenting has not been made. Withdrawal of this rejection is respectfully requested.

Regarding methods claims 151, 163 and 164, Applicants additionally note that the cited claims of the '000 application neither teach nor suggest that "expression of the GFP and the amplifiable selectable marker is indicative of the cell also expressing the desired product", as required by those claims. The Examiner did not explain in the rejection how the claims of the '000 application allegedly render obvious the rejected instant claims which require that expression of the GFP and the amplifiable selectable marker is indicative of the cell also expressing the desired product. Nor did the Examiner demonstrate that there was a reasonable expectation of success. Applicants respectfully submit that there was no reasonable expectation of success that expression of the GFP and the amplifiable selectable marker would be indicative of the cell also expressing the desired product, for the reasons stated above in the section responding to the 35 USC 103(a) rejection over Herlitschka and Tan. Accordingly, Applicants submit that this rejection is improper. Withdrawal of this rejection is respectfully requested.

Application No. 10/715,270

Claims 106-111, 138-143, 148-151 and 161-164 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 36-37, 39-41 and 47-52 of co-pending Application No. 10/715,270 ('270 application). Applicants respectfully traverse this rejection.

Applicants additionally note that claim 112 has been cancelled, and claims 113 and 114, deemed allowable in the Office Action, have been rewritten in independent form. Claim 143 has been amended and no longer references a vector of claim 106. Claims 151, 163 and 164 have been amended and now recite that the desired product comprises a polypeptide. Claims 161 and 162 have been cancelled.

A prima facie case of obviousness-type double patenting has not been made. As noted above, a prima facie case of obviousness-type double patenting requires at least that the compositions and methods as defined by *all the required* limitations of the claims of the '586 application must be compared to the compositions and methods as defined by *all the required* limitations of the claims of the instant application. It is improper to compare only one step or limitation found in claims of the instant application and claims of the '270 application, and to ignore additional limitations required by the claims of the instant application.

Applicants respectfully submit that the Office Action ignores additional limitations required by the claims of the instant application, at least as follows.

(1) Claims 36-37, 39-41 and 47-52 of the '270 application each recite "a fusion gene comprising a selectable gene and an amplifiable gene". This limitation is not present in instant claims 140-143, 148-151, and 163-164. In the rejection, the Examiner did not explain how claims in the '270 application that recite "a fusion gene comprising a first selectable gene and an amplifiable second selectable gene" allegedly render obvious the rejected instant claims, which do not recite "a fusion gene comprising a first selectable gene and an amplifiable second selectable gene". Accordingly, Applicants submit that this rejection is improper. Withdrawal of this rejection is respectfully requested.

(2) Claims 36-39 of the '270 application recite "culturing the host cell population in a selective medium, wherein the culturing is the first exposure of the host cell culture to selective conditions" and "a host cell that is capable of producing at least about 250 mg/l of the product of interest". This limitation is not present in instant claims 140-143, 148-151, and 163-164. In the rejection, the Examiner did not explain how claims in the '270 application that recite "culturing the host cell population in a selective medium, wherein the culturing is the first exposure of the host cell culture to selective conditions" and "a host cell that is capable of producing at least about 250 mg/l of the product of interest" allegedly render obvious the rejected instant claims, which do not recite "culturing the host cell population in a selective medium, wherein the culturing is the first exposure of the host cell culture to selective conditions" and "a

host cell that is capable of producing at least about 250 mg/l of the product of interest". Accordingly, Applicants submit that this rejection is improper. Withdrawal of this rejection is respectfully requested.

(3) Methods claims 40 (and claims dependent therefrom), and 47-52 of the '270 application recite "introducing a DNA construct into a population of host cells in suspension culture". This limitation is not present in instant claims 140-143, 148-151, and 163-164. In the rejection, the Examiner did not explain how claims in the '270 application that recite "introducing a DNA construct into a population of host cells in suspension culture" allegedly render obvious the rejected instant claims, which do not recite "introducing a DNA construct into a population of host cells in suspension culture". Accordingly, Applicants submit that this rejection is improper. Withdrawal of this rejection is respectfully requested.

(4) Claim 41 of the '270 application recites "culturing the host cell population in a selective medium, wherein the culturing is the first exposure of the host cell culture to selective conditions". As noted above, this limitation is not present in instant claims 140-143, 148-151, and 163-164. In the rejection, the Examiner did not explain how claims in the '270 application that recite "culturing the host cell population in a selective medium, wherein the culturing is the first exposure of the host cell culture to selective conditions" allegedly render obvious the rejected instant claims, which do not recite "culturing the host cell population in a selective medium, wherein the culturing is the first exposure of the host cell culture to selective conditions". Accordingly, Applicants submit that this rejection is improper. Withdrawal of this rejection is respectfully requested.

For the above-stated reasons, withdrawal of this rejection is respectfully requested.

SUMMARY

Applicants believe that this application is now in condition for allowance and respectfully requests that the outstanding rejections be withdrawn and this case passed to issue. The Examiner is invited to contact the undersigned at (650) 467-6222 in order to expedite the resolution of any remaining issues.

In the unlikely event that this document is separated from the transmittal letter or if fees are required, applicants petition the Commissioner to authorize charging our **Deposit Account 07-0630** for any fees required or credits due and any extensions of time necessary to maintain the pendency of this application.

Respectfully submitted,

GENENTECH, INC.

Date May 13 2006

By: Cara Coburn

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